

REMARKS

As requested by the Examiner, the title has been amended to be more commensurate with the scope of the claims.

Claims 13 and 128 have been amended to specify that the means for heating the sample is a means for heating the sample at a rate of at least 0.5°C/second, and that the means for cooling the sample is a means for cooling the sample at a rate of at least 0.5°C/second. Support for the amendments to claims 13 and 128 is found in the specification at page 52, lines 19-21.

Claims 33 and 145 have been amended to specify that the fluid is a gas. Support for the amendments to claims 33 and 145 is found in the specification at page 13, lines 13-17. Claim 55 has been amended to specify that the thermal cycling means comprises a means for heating selected from the group consisting of hot gas, a lamp, and infrared radiation and a means for cooling comprising cool air flow. Support for the amendment to claim 55 is found throughout the specification, including page 13, lines 13-17 (gas flow) and page 42, lines 5-13 (heating with lamp or with infrared radiation).

New claims 159-162 depend from claim 13 and specify additional rates of heating and cooling the PCR sample. Support for new claims 159-162 is found in the specification on page 53, lines 1-13. New claim 163 is similar to claim 13, except that new claim 163 specifies that the means for heating the sample is selected from the group consisting of hot gas, a lamp, and infrared radiation and a means for cooling comprising cool air flow. Support for new claim 163 is found in original claim 13, the specification page 13, lines 13-17 (gas flow), and page 42, lines 5-13 (heating with lamp or with infrared radiation). New claims 164 and 165 are similar to original claims 14 and 15, except depending from new claim 163. New claims 166 and 167 depend from claims 33 and 145, respectively, and specify that the gas is air. As noted by the Examiner, the specification contains lengthy discussion of heating and cooling with air. New claim 168 is similar to original claim 55, except specifying that the thermal cycling means heats

and cools the first holding means and the second holding means at a rate of at least 0.5°C/second. Support for new claim 168 is found in original claim 55 and in the specification at page 52, lines 19-21. New claims 169-172 depend from claim new claim 168 and specify additional rates of heating and cooling the PCR sample. Support for new claims 169-172 is found in the specification on page 53, lines 1-13. No new matter is added by way of any of these amendments.

Claims 13-35, 55-59, 128-146, and 156-158 stand rejected under 35 U.S.C. § 112, second paragraph as being indefinite. In particular, the Examiner questions the scope of the means-plus-function claim elements associated with heating and cooling the sample. Claims 13, 55, 128, and 145 have all been amended to provide additional limitation to the means-plus-function claim elements associated with heating and cooling the sample. Claim 13 and 128 specify the rate of heating and cooling, claims 33 and 145 have been amended to replace “fluid” with “gas,” and claim 55 has been amended to specify particular means for heating and cooling. All other rejected claims depend from claims 13, 55, 128, and 145. Accordingly, applicants respectfully request withdrawal of this rejection.

Claims 13, 14, 18, 20, 24, 25, 28, 31, 55-57, 118, 157, and 158 stand rejected under 35 U.S.C. § 102 (b) as being anticipated by Higuchi et al. (Bio/Technology 10:413 (1992)). Claim 13 (and dependent claims 14, 18, 20, 24, 25, 28, 31, 157, and 158) has been amended to specify that the means for heating the sample is a means for heating the sample at a rate of at least 0.5°C/second, and that the means for cooling the sample is a means for cooling the sample at a rate of at least 0.5°C/second. Such heating and cooling rates are not disclosed in Higuchi. Similarly, claim 55 (and dependent claims 56-57) has been amended to specify that the thermal cycling means comprises a means for heating selected from the group consisting of hot gas, a lamp, and infrared radiation and a means for cooling comprising cool air flow. None of these means for heating or means for cooling are taught in Higuchi. Applicants respectfully request

withdrawal of this rejection as it applies to claims 13, 14, 18, 20, 24, 25, 28, 31, 55-57, 157, and 158.

With respect to claim 118, applicants note that claim 118 requires a light emitting source positioned to illuminate the sample vessel along an axis substantially parallel to a wall along the second dimension of the vessel and a light detector positioned to measure fluorescence from the sample vessel along an axis substantially parallel to a wall along the second dimension of the vessel. The Eppendorf tubes of Higuchi do not have parallel walls, and there is no teaching of a light emitting source and a detector positioned to illuminate/measure fluorescence from the sample vessel along an axis substantially parallel to a wall along the second dimension of the vessel. Applicants respectfully request withdrawal of this rejection.

Claims 13, 14, 18, 20, 24, 25, 28, 31, 55, 79, 118, 157, and 158 stand rejected under 35 U.S.C. § 103 (a) as being unpatentable over Linn et al. (U.S. Patent No. 5,800,989). As discussed above, claim 13 (and dependent claims 14, 18, 20, 24, 25, 28, 31, 157, and 158) has been amended to specify that the means for heating the sample is a means for heating the sample at a rate of at least 0.5°C/second, and that the means for cooling the sample is a means for cooling the sample at a rate of at least 0.5°C/second. Such heating and cooling rates are not disclosed in Linn. Also as discussed above, claim 55 has been amended to specify that the thermal cycling means comprises a means for heating selected from the group consisting of hot gas, a lamp, and infrared radiation and a means for cooling comprising cool air flow. Such thermal cycling means are not taught or suggested in Linn. Applicants respectfully request withdrawal of this rejection as it applies to claims 13, 14, 18, 20, 24, 25, 28, 31, 55, 157, and 158.

With respect to claims 79 and 118, both of these claims require the sample vessel to have first and second dimensions wherein the first dimension is less than the second dimension. Furthermore, claims 79 and 118 requires a light emitting source positioned to illuminate the sample vessel along an axis substantially parallel to a wall along the second

dimension of the vessel and a light detector positioned to measure fluorescence from the sample vessel along an axis substantially parallel to a wall along the second dimension of the vessel. As with Higuchi, Linn does not teach of a light emitting source and a detector positioned to illuminate/measure fluorescence from the sample vessel along an axis substantially parallel to a wall along the vessel. Moreover, Linn does not teach measuring along the second (longer) dimension of the vessel. Applicants respectfully request withdrawal of this rejection.

Finally, the disclosure stands objected to because of a misspelling on page 34, line 16. The specification has been amended accordingly.

CONCLUSION

The application as amended, is believed to be in condition for allowance. Withdrawal of the rejections and passage of the application to issuance is requested.

Respectfully submitted,



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Appendix A
Version with markings to show changes made

Under 37 C.F.R. § 1.121(b), please rewrite the title as follows:

SYSTEM AND METHOD FOR FLUORESCENCE MONITORING [PCR
PROCESS]

Also, please amend the paragraph beginning on page 34, line 10, as follows:

The polymerase chain reaction was run in a 10 µl volume with 50 ng of human genomic template DNAes, 0.5 mM of each deoxynucleotide, 500 nM of each of two oligonucleotide primers GGTTGGCCAATCTACTCCCAGG (SEQ ID NO:5) and GCTCACTCAGTGTGGCAAAG (SEQ ID NO:6) in a reaction buffer consisting of 50 mM Tris-HCl (pH 8.5 at 25°C), 3.0 mM magnesium chloride, 20 mM KCl, and 500 µg/ml bovine serum albumin. *Thermus [aquatics] aquaticus* DNA polymerase (0.4 µ) was added, the samples placed in 8 cm long, thin-walled capillary tubes (manufactured by Kimble, Kimax 46485-1), and the ends fused with a laboratory gas burner so that an air bubble was present on both ends of each tube.

Under 37 C.F.R. § 1.121(c)(1)(i), please amend claims 13, 33, 55, 128, and 145 as follows:

13. (Thrice Amended) A system for performing PCR and monitoring the reaction during temperature cycling comprising;

a sample container for holding a PCR sample, the sample container comprising an optically clear material, the sample container formed for holding less than 1 milliliter of a sample and having a first side, a second side, and an end;

means for positioning the PCR sample container in a monitoring position;

means for heating the PCR sample at a rate of at least 0.5°C/second;

means for cooling the PCR sample at a rate of at least 0.5°C/second;

control means for repeatedly operating the means for heating and the means for cooling to subject the PCR sample to thermal cycling;

means for optically exciting the to cause the sample to fluoresce; and

means for detecting the fluorescence of the excited sample during amplification

when the sample is in the monitoring position.

33. (Twice Amended) A system for performing PCR and monitoring the reaction in real time during temperature cycling comprising:

a plurality of sample containers for holding a plurality of PCR samples, each sample container comprising an optically clear capillary tube, each sample container formed for holding less than 1 milliliter of a sample and having a sealed end and an open end with a sealable closure on the open end;

means for holding a plurality of sample containers, the means for holding comprising a rotatable carousel formed for holding the sample containers;

means for forcing hot [fluid] gas into contact with the plurality of sample containers;

means for forcing cool [fluid] gas into contact with the plurality of sample containers;

means for repeatedly operating the means for forcing hot [fluid] gas and the means for forcing cool [fluid] gas to subject the PCR samples to thermal cycling; means for optically exciting at least one selected PCR sample to cause the selected PCR sample to fluoresce; means for detecting the fluorescence of the excited selected PCR sample at both a first wavelength and a second wavelength; and means for determining at least one reaction parameter for the selected PCR sample in accordance with the fluorescence at the first and second wavelengths and displaying the reaction parameter in a visually perceptible manner in real time.

55. (Twice Amended) A system for carrying out and monitoring the progress of first and second biological reactions comprising:

first holding means for holding a first biological sample; second holding means for holding a second biological sample; transporting means for moving the first and second holding means between a non-monitoring position and a monitoring position; thermal cycling means for repeatedly heating and cooling the first holding means and the second holding means in both the non-monitoring position and in the monitoring position to carry out thermal cycling on both the first biological sample and the second biological sample, the thermal cycling means comprising a means for heating selected from the group consisting of hot gas, a lamp, and infrared radiation and a means for cooling comprising cool air flow; monitoring means for ascertaining the progress of the first biological reaction in the first means for holding and the second biological reaction in the second means for holding when the first and second biological samples are in the monitoring position, the means for

monitoring comprising means for detecting radiation emitted from the first and second biological samples; and

controlling means for controlling the operation of the transporting means, thermal cycling means, and the monitoring means such that the progress of the first and second biological reactions is detected as thermal cycling occurs.

128. (Twice Amended) A system for performing PCR and monitoring the reaction during temperature cycling comprising;

a sample container for holding a PCR sample, the sample container comprising an optically clear material, the sample container formed for holding less than 1 milliliter of a sample and having a first side, a second side, and an end;

means for positioning the PCR sample container in a monitoring position;

means for heating the PCR sample at a rate of at least 0.5°C/second;

means for cooling the PCR sample at a rate of at least 0.5°C/second;

control means for repeatedly operating the means for heating and the means for cooling to subject the PCR sample to thermal cycling;

means for optically exciting the sample to cause the sample to fluoresce;

means for detecting the fluorescence of the excited sample during amplification when the sample container is in the monitoring position;

means for determining at least one reaction parameter in accordance with the detected fluorescence; and

means for adjusting the control means in accordance with the reaction parameter.

145. (Amended) A system for performing PCR and monitoring the reaction in real time during temperature cycling comprising:

a plurality of sample containers for holding a plurality of PCR samples, each sample container comprising an optically clear capillary tube, each sample container formed for holding less than 1 milliliter of a sample and having a sealed end and an open end with a sealable closure on the open end;

means for holding a plurality of sample containers, the means for holding comprising a rotatable carousel formed for holding the sample containers;

means for forcing hot [fluid] gas into contact with the plurality of sample containers;

means for forcing cool [fluid] gas into contact with the plurality of sample containers;

means for repeatedly operating the means for forcing hot [fluid] gas and the means for forcing [fluid] gas fluid to subject the PCR samples to thermal cycling;

means for optically exciting at least one selected PCR sample to cause the selected PCR sample to fluoresce;

means for detecting the fluorescence of the excited selected PCR sample at both a first wavelength and a second wavelength;

means for determining at least one reaction parameter for the selected PCR sample in accordance with the detected fluorescence at the first and second wavelengths and displaying the reaction parameter in a visually perceptible manner in real time; and

means for adjusting the means for repeatedly operating in accordance with the reaction parameter such that the reaction is adjusted in real time.